WO 2005/049595

CLAIMS

- 1. A process for the preparation of citalopram characterized in that: (a) 5-cyanophthalide is treated with a mixture of 4-fluorophenyl magnesium halide and 3-dimethylaminopropyl magnesium halide and (b) the obtained mixture is treated with an organic acid, an inorganic acid, a phosphine, or with a labile ester forming group and a base.
- 2. A process according to claim 1, characterized by the use of from 1.8 to 2.0 moles of 4-fluorophenyl magnesium halide, preferably about 1.8, for each mole of 5-cyanophthalide.
- 3. A process according to claim 1, characterized by the use of from 1.09 to 1.2 moles of 3-dimethylaminopropyl magnesium halide, preferably about 1.1, for each mole of 5-cyanophthalide.
- 4. A process according to claim 1, characterized by the fact that from 1.7 to 1.6 moles of 4-fluorophenyl magnesium halide, preferably about 1.64, are used for each mole of 3-dimethylaminopropyl magnesium halide.
- 5. A process according to claims 1-4, characterized by the fact that 4-fluorophenyl magnesium halide is a bromide.
- 6. A process according to claims 1-4, characterized by the fact that 3-dimethylaminopropyl magnesium halide is a chloride.
- 7. A process according to any one of the previous claims, characterized by the fact that said acid has a pK comprised from 0 to 3, preferably from 2 to 3.
- 8. A process according to claim 7, characterized by the fact that said acid is orto-phosphoric acid.
- 9. A process according to claims 7-8, characterized by the fact that the acid is used in a concentration comprised from 55 to 95% by weight, preferably in concentration of about 85% by weight.
- 10. A process according to claims 1-6, characterized in that the phosphine is thriphenylphosphine.
- 11. A process according to claims 1-6, characterized in that the labile ester forming group is selected from the halide or the anhydride of an organic acid.

- 12. A process according to claim 11, characterized in that the halide of the organic acid is the halide of methanesulfonic, p-toluenesulfonic, trifluoroacetic or trifluoromethanesulfonic acid.
- 13. A process according to claim 12, characterized in that the halide is the chloride.
- 14. A process according to claims 11-13, characterized in that base is selected from triethylamine, dimethylaniline or pyridine.
- 15. A process according to any one of the previous claims, characterized by the fact that the process is carried out in an organic polar aprotic solvent.
- 16. A process according to claim 15, characterized by the fact that the process is carried out in from 1.0 to 1.6 litres of solvent, preferably in about 1.2 litres, for each mole of 5-cyanophthalide.
- 17. A process according to claims 15-16, characterized by the fact that the solvent is selected from tetrahydrofuran and/or toluene.
- 18. A process according to any one of previous claims, characterized by the fact that the step (a) is carried out at -20÷+20°C, preferably at -10÷0°C.
- 19. A process according to any one of previous claims, characterized by the fact that the step (b) is carried out at -10:+20°C, preferably at 0:+10°C.
- 20. A process according to any one of previous claims, characterized by the fact of being carried out without isolating the intermediate products.
- 21. Compound of formula:

where X is an halogen, preferably chlorine or bromine.

17. Use of a compound according to claim 21 as an intermediate in the preparation of citalogram.